

-continued

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21

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20

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**1-50. (canceled)**

**51.** A method of treating a cancer comprising administering a therapeutically effective amount of an anti-Gremlin-1 (GREM1) antagonist to a subject in need thereof.

**52.** The method according to claim **51**, wherein:

- (a) the cancer is a solid cancer;
- (b) the cancer has stromal GREM1 overexpression; and/or
- (c) the cancer is selected from colorectal cancer, multiple myeloma, pancreatic cancer, bladder cancer, breast cancer, lung cancer, stomach cancer, duodenal cancer, oesophageal cancer, head and neck cancer, prostate cancer, glioma, endometrial cancer, liver cancer, spleen cancer, bone-resident cancer, and osteosarcoma.

**53.** The method according to claim **52**, wherein the cancer is colorectal cancer; optionally wherein the colorectal cancer is a mesenchymal subtype colorectal cancer.

**54.** The method according to claim **52**, wherein the cancer is multiple myeloma.

**55.** The method according to claim **52**, wherein the cancer is breast cancer.

**56.** The method according to claim **51**, wherein the cancer has epithelial GREM1 overexpression; optionally wherein the cancer is a GREM1-initiated cancer.

**57.** The method according to claim **51**, wherein:

- (a) the cancer is a disseminated cancer; and/or
- (b) the cancer is an established cancer, optionally wherein the established cancer is an established colorectal cancer.

**58.** The method according to claim **51**, wherein the antagonist is a peptide, a protein, an antibody, a polynucleotide, an oligonucleotide, an antisense RNA, a small interfering RNA (siRNA), a small molecule inhibitor or a small hairpin RNA (shRNA).

**59.** The method according to claim **58**, wherein the antagonist is an anti-Gremlin-1 antibody comprising a HCDR1/HCDR2/HCDR3/LCDR1/LCDR2/LCDR3 sequence combination of SEQ ID NOs: 4/5/6/7/8/9 or SEQ ID NOs: 3/5/6/7/8/9.

**60.** The method according to claim **58**, wherein the anti-Gremlin-1 antibody comprises a heavy chain variable region (HCVR) sequence of SEQ ID NO: 10 or 12 and/or a light chain variable region (LCVR) sequence of SEQ ID NO: 11 or 13; optionally wherein the anti-Gremlin-1 antibody comprises a HCVR and LCVR sequence pair of SEQ ID NOs: 10/11 or 12/13.

**61.** The method according to claim **60**, wherein the anti-Gremlin-1 antibody comprises a heavy chain of SEQ ID NO: 14, 16, 18, 22, 28, 30, 32 or 34 and/or a light chain of SEQ ID NO: 15, 17, 19, 23, 29, 31, 33 or 35; optionally wherein the anti-Gremlin-1 antibody comprises a heavy and light chain pair of SEQ ID NOs: 14/15, 16/17, 18/19, 22/23, 28/29 or 30/31, 32/33, 34/35.

**62.** The method according to claim **58**, wherein:

- (a) the antagonist is an antibody which competes for binding to Gremlin-1 with an anti-Gremlin-1 antibody comprising a HCDR1/HCDR2/HCDR3/LCDR1/LCDR2/LCDR3 sequence combination of SEQ ID NOs: 4/5/6/7/8/9 or SEQ ID NOs: 3/5/6/7/8/9; or
- (b) the antagonist is an antibody which binds the same epitope on Gremlin-1 as an anti-Gremlin-1 antibody comprising a HCDR1/HCDR2/HCDR3/LCDR1/LCDR2/LCDR3 sequence combination of SEQ ID NOs: 4/5/6/7/8/9 or SEQ ID NOs: 3/5/6/7/8/9.

**63.** The method according to claim **58**, wherein:

- (a) the antagonist antibody is a chimeric, human or humanised antibody; and/or